US Army Medical Research and Materiel

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Recombinant Light Chains of Botulinum Neurotoxins and Light Chain Fusion Proteins for Use in Research and Clinical Therapy

Features and advantages:

- ***E. coli* expression system produces large quantities of nontoxic LC from BoNT/A**
- **High level of expression enables easy purification and extensive characterization**
- **BoNT/A LC preparation can elicit protective immunity in mice**
- **Provides cost savings**
- **biological containment facilities**

Patent Status

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This invention provides for the construction, expression, and purification of synthetic DNA molecules that encode polypeptides comprising botulinum neurotoxin (BoNT) light chains (LC). The invention also includes methods of vaccination against botulism using the expressed peptides.

BoNTs are expressed as single polypeptides containing a disulfide bond between the N-terminal LC and C-terminal heavy chain (HC). The invention is based, in part, on modifying the wild-type BoNT sequence according to the codon usage normally found in genes that are highly expressed in the host organism. By selecting codons rich in G+C content, the synthetic DNA molecules may further be designed to lower the high A+T rich base composition found in clostridial genes. The BoNT LC may be expressed in a heterologous host system by itself or be fused to another protein or carrier, for example to a synthetic or wild-type BoNT HC or a fragment thereof.

Clostridium botulinum causes botulism by producing BoNTs which block the transmission of neuromuscular stimuli. It only takes a few BoNT molecules to stop nerve cell activity, leading to respiratory failure and death. Humans are naturally affected by BoNTs via food [illegible]g, infant botulism, and wound botulism. [illegible]n poisoning could also occur during biological warfare. Seven different antigenically distinct serotypes (A - G) of BoNTs have been characterized. The invention provides for the high level expression of gram quantities of LC from BoNT serotype A (BoNT/A) in *E. coli*. The [illegible]tion was highly soluble, stable at 4° C for 6 months and had the expected enzymatic and functional properties.

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